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Equine cardiovascular pathology: an overview

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Abstract

The few data collections that evaluate the involvement of organ systems in horse diseases are in agreement that the locomotor, gastrointestinal and nervous systems are the sites of primary disease in the vast majority of sick horses. When compared with diseases of these organ systems, equine cardiovascular diseases occur infrequently. The most detailed and comprehensive survey of equine cardiac pathology was reported in 1972 by Else and Holmes, who summarized the gross and microscopic cardiac findings from 1500 abattoir horses. This paper reviews the pathology of the cardiovascular diseases typically encountered in horses. Most of the pathological examples are from the files of the Veterinary Medical Teaching Hospital at the University of Florida, encompassing 24 years (1978–2002) and some 6000 equine necropsy cases. Preceding the specific topics are principles of the anatomy and function of the normal equine heart. Pathological entities include equine congenital cardiovascular diseases, acquired diseases of the pericardium, myocardium, endocardium and valves, cardiac neoplasms, and common equine vascular diseases and vascular neoplasms. Extensive use is made of photographs to illustrate the features of individual case examples.

Keywords: normal heart, heart dissection, cardiac enzymes and stains, congenital disorders, epicardial, myocardial, endocardial and valvular diseases, vascular diseases, tumors

Introduction

In the horse, cardiovascular diseases are relatively infrequent compared with diseases of other organ systems. Likewise, reviews of the pathology of the equine cardiovascular system are rare in the literature. Yet a healthy heart is necessary for the many functions of all organ systems and is especially important for the equine athlete.

This article summarizes pathological aspects of equine cardiovascular diseases, including congenital disorders, acquired pericardial, myocardial and endocardial–valvular diseases, common vascular diseases and primary neoplasms affecting the equine heart and the vessels. Principles of human structural cardiac abnormalities are added to support the understanding of similar aspects of equine cardiopathology when the pathogenesis is poorly understood in this species. The overview is preceded by an account of the principles of the morphology and function of the non-diseased equine heart and guidelines for a systematic gross dissection of the heart. The article is not intended to cover clinical aspects of the diseased equine heart, as in some instances a blend of structural, functional and biological changes can account for the progression of heart disease.

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The normal equine heart

The equine heart occupies the ventral part of the middle mediastinal space, extending between ribs 2 and 6 (Quiring and Baker, 1953; Littlewort, 1986; Hanson *et al.*, 1994). It is enveloped by the pericardium, in which it

freely moves, and is bathed by approximately 20 ml of a straw-colored transparent fluid. The pericardium is tightly attached to the sternum. The weight of the equine heart is determined by breed type (draft versus racing), sex and age. Generally it averages 0.6% of the total body weight (about 4 kg) in horses without exercise (Hanson *et al.*, 1994). Horses under training and exercise respond with a heart weight generally greater than 0.6% of the total body weight (Physick-Sheard, 1985). The heart weight of the Thoroughbred horse ranges between 0.85% and 1.0% of the body weight (Evans, 1985; Gunn, 1989). Training of equine athletes induces concentric physiological ventricular hypertrophy.

The shape of the equine heart resembles that of a cone with a distinct apex formed by the left ventricle. The equine heart is composed of two ventricles and two atria, the aorta exiting from the left ventricle and the pulmonary trunk from the right ventricle. The bulk of the heart is made up of the myocardium, which is covered on the outside by the visceral layer of the pericardium (defined as the epicardium) and which is lined internally by the endocardium, a thin, translucent and glistening membrane. The fibrous ring (annulus fibrosus) separates the musculature of the atria from that of the ventricles. The aortic fibrous ring of older horses frequently contains a plate of cartilage.

There are four sets of heart valves: two contributing to the atrioventricular valves (mitral and tricuspid) and two to the semilunar valves (aortic and pulmonary) (Quiring and Baker, 1953). The mitral valve or bicuspid valve is attached to the fibrous ring surrounding the left atrioventricular orifice and has one cranial and one caudal leaflet. Each mitral valve leaflet receives chordae tendineae from both papillary muscles. The tricuspid valve has three leaflets (cranial, septal and right). The aortic valve consists of three semilunar cusps. Each cusp has a normal, small, firm nodule in the center of the free edge known as the corpus arantii. The junctions of the cusps with each other laterally are known as commissures. The space (pocket) between the intima of the aorta (and also of the pulmonary trunk) and the cusps of both sets of semilunar valves is known as the sinus of Valsalva. The aortic semilunar valves are close to the origin of the right and left coronary arteries, which arise opposite the cranial and left caudal cusps respectively. The pulmonary valve, smaller and thinner than the aortic valve, consists of three semilunar cusps: cranial, right caudal and left caudal. The corpora arantii are less prominent here.

The inside of both ventricles is composed of papillary muscles, moderator bands, chordae tendineae and muscular trabeculae carneae. The atria contain trabeculated or pectinate muscles.

The heart is an organ with a constant number of muscle cells under physiological conditions. It is a pump that supplies oxygenated blood to the body and recycles venous blood from the body to the lungs (Littlewort, 1986). It is connected to two independent, yet integrated circulatory circuits: the systemic and pulmonary circulations. The innervation of the heart is derived from the sympathetic and parasympathetic divisions of the autonomic nervous system (McKibbe and Getty, 1969). In addition to external sources, the heart receives electrical stimuli from structural centers known as the sinoatrial node, the atrioventricular node and the bundles of His, specialized nervous and muscular tissues acting as a conduction system. Finally, the heart is considered an endocrine organ in that hormone-producing cardiocytes are located within both atria. These secrete a peptide hormone known as atrial natriuretic factor (ANF) (Cantine and Genest, 1986). This hormone plays an important role in the regulation of blood pressure and blood volume, and in the excretion of water, sodium and potassium. ANF is considered an antagonist of the renin–angiotensin system in the control of the initial phases of congestive heart failure. In the horse, as in other species, hormone production has been morphologically characterized in the cytoplasm of atrial cardiocytes as secretory granules (Mifune *et al.*, 1995; Richter *et al.*, 1998). The hormone exists as a prohormone in these equine structures, and the gene for the precursor protein has been cloned. The hormone is cleaved to its active form simultaneously with its secretion. The function of ANF has been studied in horses exposed to exercise and heat (Kokkonen *et al.*, 1995, 1999).

Dissection of the equine heart

The heart muscles usually undergo rigor mortis within 1–2 h after death (Rooney and Robertson, 1996). Blood will be trapped in both ventricles following rigor and may clot.

There are several methods of systematic dissection of the heart (Turk and Root, 1983; Maxie, 1991; Buergelt and Young, 1992). Care should be taken not to mutilate major cardiac structures, regardless of which method is chosen. Recommended tools are a knife with a straight blade, long straight scissors and a flexible ruler to take cardiac measurements. Rinsing water should be readily available.

The method of cardiac dissection taught at the University of Florida is as follows. The heart and lungs are removed together with the entire pluck from the thorax. The pericardial sac is opened through a small incision to assess the volume and nature of the straw-colored pericardial fluid (normally 10–20 ml). A sample of fluid is obtained for culture or cytology when necessary. Fluid collection can be done *in situ* before removal of the pluck. The heart is then freed from its vascular suspensions (aorta, pulmonary trunk, veins). At this point, one should check for anomalous origin of the

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great vessels and their primary branches. The left and right heart sides should be identified before the atria and ventricles are opened. The pointed cardiac apex clearly designates the left ventricle. The pulmonary outflow tract is identified and carefully incised. The pulmonary semilunar valves are inspected. Should a patent ductus arteriosus be suspected, the patent ostium into the pulmonary outflow should be examined and the connection to the aorta nearby can be verified with a probe.

The first incision is extended caudally into the right ventricle. The knife or scissors are turned at an angle of 180° and the incision is continued parallel to the interventricular septum towards the right atrium. Closure of the foramen ovale is visualized by opening the caudal vena cava. The left ventricle is opened longitudinally from the free lateral side, starting slightly above the apex. The cut is directed towards the left atrium, the tip of the knife passing underneath the septal mitral valve leaflet towards the aortic ostium. A focal cartilaginous structure that becomes mineralized in older horses, and is termed cartilago cordis, is normally located in the left heart of the horse at the transition from the upper ventricle into the atrium, and may be difficult to cut with a knife. The mitral valve leaflet is severed and the ascending aorta is opened. The appearance of the endocardium, valves, chordae tendineae and papillary muscles is recorded after rinsing off any residual clotted blood that may have been trapped within the atria and ventricles. Moderator bands and trabeculae carneae are more numerous in the right ventricle than in the left (Quiring and Baker, 1953). The papillary muscles in the left ventricle are better developed than those in the right ventricle (Quiring and Baker, 1953).

The entire heart can be weighed now. The circumference of each valve ring can be measured with a flexible ruler, as can the free ventricular wall thickness at the midpoint of its longitudinal axis. The degree of myocardial contraction and its integrity can be determined by slicing tangentially into the myocardial muscle mass. Tissue samples for routine microscopic examination should be obtained from all four chambers. These should be cut into small cubes, measuring 1 × 1 × 0.5 cm, and should be submerged in adequate volumes of 10% buffered neutral formalin. Additional tissues are taken from sites of pathological changes (Palate *et al.*, 1995). In particular, planes of sectioning should facilitate examination of the specialized myocyte components of the conducting system (Palate *et al.*, 1995).

Histological stains

Stains for the histological evaluation of myocardial diseases include hematoxylin–eosin for initial orientation. Special stains such as Masson's trichrome specifically demonstrate fibrin, muscle and connective tissue. Normal myocardium stains red, while damaged myocardium stains gray–purple with this special stain. Phosphotungstic acid–hematoxylin (PTAH) is used to demonstrate microthrombi and loss of myocyte striations. Van Gieson stain shows fibrils and connective tissues, while hematoxylin–basic fuchsin–picric acid (HBFP) demonstrates myocyte necrosis. Immunohistochemistry and electron microscopy are additional diagnostic tools.

Cardiac enzymes

Cardiac enzymes are of limited use in equine cardiovascular medicine as they are unreliable for diagnosis. In recent years immunoassays have been developed in human patients to measure serum levels of troponin T and troponin I as cardiac markers (O'Brian *et al.*, 1997, 1998; Lindahl *et al.*, 2000). Together with troponin C, these myocardial proteins regulate the calcium-dependent interaction between myosin and actin to produce systematic cardiac contraction and relaxation. Deterioration of the contractile apparatus and increased membrane permeability after myocyte death cause the release of troponins into the serum. Whereas the identical troponin C protein is expressed by cells in both cardiac and skeletal muscle, the amino acid sequence of troponin T and troponin I in cardiac muscle differs from that in skeletal muscle. The difference in amino acid sequence has allowed the development of monoclonal antibodies against cardiac troponins T and I that can be used in an enzyme-linked immunosorbent assay (troponin T) or immunoassay (troponin I) to specifically identify early myocardial cell necrosis. Immunoassays have been developed to measure troponin T and troponin I in a range of animal species, including the horse (O'Brian *et al.*, 1997, 1998; Cornelise *et al.*, 2000).

The pathology of the diseased equine heart

Various schematic classifications of cardiac disease categories have been proposed in the journal literature and in textbooks (Robinson and Maxie, 1993; Rooney and Robertson, 1996; Patteson, 1996; Colahan *et al.*, 1999). In this overview heart diseases are classified as congenital malformations, diseases of the pericardium, diseases of the myocardium, diseases of the mural endocardium, diseases of the valves, commonly occurring diseases of the vessels, and cardiac and vascular tumors. Acquired primary causes of heart diseases will be divided into degenerative, inflammatory and neoplastic categories.

The literature contains one comprehensive survey of equine gross and microscopic cardiac pathology summarizing a total of 1507 British abattoir horses in 1972 (Else and Holmes, 1972a, b). As this study dealt mainly with working horses, the statement in it that valvular lesions

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were most frequently encountered in the aortic semilunar valves and contributed to 25% of all cardiovascular changes might be considered biased. A comprehensive report on heart murmurs in 846 racehorses correlated clinical findings with performance (Kriz *et al.*, 2000).

Congenital cardiovascular diseases

Congenital cardiac anomalies in the horse may account for 3–5% of all congenital organ defects (Reef, 1985; Cottrill and Rossdale, 1992; Rooney and Robertson, 1996). Not all horses with congenital cardiovascular lesions show clinical signs, but the clinical signs induced by congenital equine heart diseases include stunting, exercise intolerance, murmurs, circulatory overload, respiratory distress and cyanosis. Defects of the interventricular septum are the most commonly reported congenital malformations in the horse and are diagnosed in nearly 50% of the cases belonging to this category (Reef, 1985). Other single congenital anomalies reported in the horse's heart include atrial septal defects and persistent foramen ovale. Primary vascular anomalies in horses include anomalous origin of the left coronary artery (Karlstam *et al.*, 1999), persistent right aortic arch (Butt *et al.*, 1998) and persistent ductus arteriosus (Carmichael *et al.*, 1971; Reimer *et al.*, 1993). Complex equine cardiovascular anomalies have been documented, such as tetralogy of Fallot (Reynolds and Nicholl, 1978; Keith *et al.*, 1981; Cargile *et al.*, 1991), common truncus arteriosus (Sojka, 1987; Steyn *et al.*, 1989), transposition of the greater arteries (Vitums *et al.*, 1973) and double-outlet right ventricle (Chaffin *et al.*, 1992). Valvular anomalies in the equine heart mainly affect aortic semilunar valves (stenosis, fibrosis) and the tricuspid and mitral atrioventricular valves (dysplasia) (Meurs *et al.*, 1997). Individual case reports in the literature deal with various concurrently occurring cardiovascular abnormalities (Hadlow *et al.*, 1980; Bayley *et al.*, 1982; Zamora, 1985; Glazier, 1986; Reppas *et al.*, 1996; Spiro, 2002).

Clinically, cyanosis may be one of the hallmarks in foals and young horses that lead to suspicion of the presence of shunting of arterial and venous blood due to significant communications in the heart. In cases of tetralogy of Fallot, cyanosis from mixing of arterial and venous blood may be present early in the life of the neonatal foal. Likewise, mixing of blood leading to cyanosis can occur in common truncus arteriosus. Transposition of the greater arteries without communication via a foramen ovale, ventricular septal defect or patent ductus arteriosus is incompatible with postnatal life. Cyanosis can be expected if these communications develop. Table 1 lists intrinsic cyanotic, potentially cyanotic and acyanotic cardiovascular malformations.

A total of 32 congenital anomalies (0.5%) out of 6500 equine necropsy accessions were retrieved from the files of the Veterinary Medical Teaching Hospital, University of Florida, for the period 1978–2002 (Table 2). Most of the single or complex anomalies were present in foals days or months old. They involved all equine breeds and no gender preference was observed. Single malformations were frequently complicated by other cardiac malformations or other organ malformations. One-third (11 cases) of the file cases involved a high ventricular septal defect followed by anomalies associated with the atrial septum (five cases) and patent ductus arteriosus (four cases). With regard to the latter two anomalies,

Table 1. Cardiovascular malformations with and without cyanosis

Acyanotic	Potentially cyanotic	Cyanotic
Persistent right aortic arch	Patent ductus arteriosus	Tetralogy of Fallot
Pulmonic stenosis	Ventricular septal defect	Persistent truncus
Aortic stenosis	Atrial septal defect	Complete transposition of arterial trunks
Atrioventricular valve dysplasia		

Table 2. Summary of cardiovascular malformations, Veterinary Medical Teaching Hospital, University of Florida, 1978–2002

Type	Age range	Degree	No. of cases
VSD	11 days to 6 months	6 single, 5 complex	11
ASD/PFO/FO	3 days to 2 months	2 single, 3 complex	5
PDA	3 days to 1.5 months	1 single, 3 complex	4
Tricuspid value agenesis	5 days to 1.5 months	–	2
Tetralogy	1 day to 3 years	–	2
Eisenmenger's	1 month	–	1
Common truncus	3 days to 6 months	–	3
Double outlet	2 years to 6 years	–	4
Total			32

VSD, ventricular septal defect; ASD, atrial septal defect; PFO, persistent foramen ovale; FO, foramen ovale; PDA, persistent ductus arteriosus.

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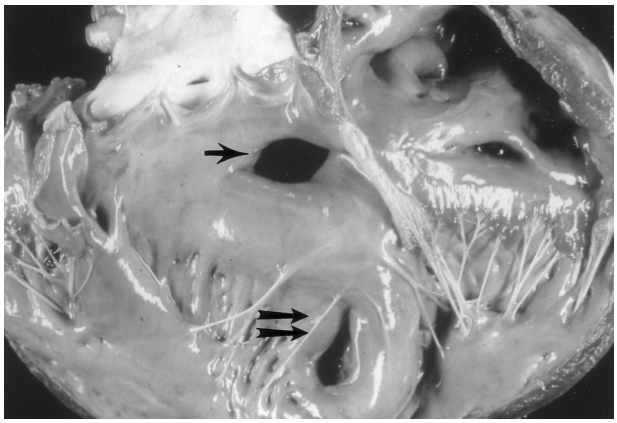

Fig. 1. Ventricular septal defects in the left ventricle of a 2-month-old Thoroughbred colt. One defect involves the subaortic membranous (single arrow) and another is present in the apical muscular portion (double arrow) of the ventricular septum.

one should be aware that anatomical closure of the foramen ovale and patent ductus arteriosus does not occur immediately after birth, whereas physiological closure should occur at that time. During fetal circulation, both an open atrial connection and a patent ductus arteriosus are the hemodynamic prerequisites for blood to bypass the lung. Shortly after birth, two independent but connected circulatory systems are established: the pulmonary and the systemic circulations.

Ventricular septal defect (VSD)

This is the most frequently encountered single cardiac defect in the horse (Lombard *et al.*, 1983; Reef, 1985). High membranous and apical muscular ventricular septal defects can both occur (Fig. 1). A resulting systolic murmur is best heard on the right side. Depending on the size of the VSD, there may be evidence of left-to-right blood shunting leading to right ventricular hypertrophy; reversal of flow leads to cyanosis. Small defects, particularly small subaortic ventricular defects, are usually well tolerated and asymptomatic. Animals with VSD may range from birth to 2 years and older.

Atrial septal defect (ASD)

An atrial septal defect is defined as an interatrial communication through which blood may flow in either direction. Abnormal embryological development of the interatrial septum may result in three types of true ASD: ostium secundum, ostium primum and sinus venosus. Ostium secundum is the most common type of ASD in humans and horses (Taylor *et al.*, 1991). It involves the central region of the atrial septum at the fossa ovalis. Ostium primum is another form of interatrial communication resulting from failure of the foramen ovale to close after birth (MacDonald *et al.*, 1988). Excessive flow from the left to the right atrium and subsequent volume overload to the right heart is an uncommon occurrence, and thus clinical signs from such overload are rare. A systolic murmur may be detected because of the increased quantity of blood flowing through the pulmonary conus.

Patent ductus arteriosus (PDA)

The ductus arteriosus is a tubular muscular structure of the fetal circulation that connects the pulmonary trunk with the ascending aorta and allows blood to bypass the lungs. In the horse it closes physiologically within 3 days after birth, is obliterated, and becomes the ligamentum arteriosum (Machida *et al.*, 1988). A ductus that fails to close in the horse more than several (3) days post-partum remains permanently patent in most cases (Machida *et al.*, 1988). The anomaly is rare in horses. The few reported cases occur mainly in foals, though individual case reports also exist for adult horses (Carmichael *et al.*, 1971; Reimer *et al.*, 1993; Spiro, 2002). The length and diameter of the ductus may vary from case to case. In order to visualize the patent ductus, the pericardium has to be dissected from the heart. There is usually a left-to-right shunting of blood with pulmonary circulatory overload and a characteristic continuous murmur on auscultation. Pulmonary hypertension in longstanding cases may lead to shunt reversal, cyanosis and aneurysm of the pulmonary artery.

Common truncus arteriosus

This anomaly is defined as one arterial vessel leaving the ventricular part of the heart (Sojka, 1987; Steyn *et al.*, 1989). It is the result of a failure of the spiral aortic–pulmonary septum to form during organogenesis. The truncus usually arises from both ventricles, but it may arise exclusively from the right ventricle. The single vessel receives predominantly unoxygenated blood through a high defective ventricular septum. Coronary arteries arise from the truncus arteriosus. Pulmonary arteries also branch off the truncus arteriosus. The number of semilunar cusps varies from three to four. The condition is cyanotic.

Tetralogy of Fallot

This is a complex malformation with high VSD, dextraposition (over-riding) of the aorta, pulmonary stenosis and right ventricular hypertrophy. The condition is accompanied by cyanosis, polycythemia and a systolic murmur (Reynolds and Nicholls, 1978; Keith, 1981; Cargile *et al.*, 1991). The severity of cyanosis depends on the degree of pulmonary stenosis. Eisenmenger's complex is similar to tetralogy of Fallot but has no pulmonary stenosis. This condition also potentially leads to cyanosis. The definitive diagnosis of either anomaly is obtained through cardiac ultrasonography and catheterization.

Complete transposition of the greater vessels

In this congenital malformation, the right ventricle pumps venous blood into the aorta, and the left

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ventricle ejects oxygenated blood back through the pulmonary arteries. The hemodynamic consequences are incompatible with postnatal life unless a connection between the left and right heart exists. If a patent ductus arteriosus or an atrial or ventricular septal defect is present, cyanosis develops, but postnatal survival may be possible for a period. Individual equine case reports of such defects have appeared in the literature (Vitums *et al.*, 1973).

Double-outlet right ventricle

This is a specific type of vascular malformation in which the aorta and the pulmonary trunk both originate from the anatomical right ventricle. Coronary arteries originate from the right aortic sinus. Pulmonary hypertension is a complication of the condition. The literature contains individual case reports of such malformation in the horse (Chaffin *et al.*, 1992). There are four such cases on file at the University of Florida.

Tricuspid valve atresia

There are several equine case reports in the literature (Hadlow and Ward, 1980; Meurs *et al.*, 1997). The condition leads to cyanosis, polycythemia and a holosystolic murmur.

Pericardial diseases

Pericardial disease involves the visceral surface of the pericardial sac and the epicardial surface of the heart. Cases of effusive non-neoplastic pericarditis, fibrinous pericarditis and rare neoplastic pericardial disorders associated with excessive fluid have been reported in the horse (Carrime *et al.*, 1977; Dill *et al.*, 1982; Foss, 1985; Freestone *et al.*, 1987; Bernard *et al.*, 1990; Buergelt *et al.*, 1990; Worth and Reef, 1998). Primary sources for pericarditis include hematogenous spread of chronic infection, spread of an inflammatory process from the pleural cavity, and penetrating chest wounds. The cause of the effusive, often non-septic form of pericarditis in the horse is unknown; *Actinobacillus equuli*, *Arcanobacterium pyogenes*, beta-hemolytic streptococci and Gram-negative rods may cause fibrinous pericarditis.

Effusive pericarditis

Fluid accumulation in the pericardium can measure up to 6 liters. The fluid is sterile and straw-colored or red depending on the number of red blood cells present. Its protein content can range between 3.5 and 6.5 g/dl (Foss, 1985; Freestone *et al.*, 1987). On cytological examination, the sediment may contain a few neutrophils, eosinophils or inactive mesothelial cells. There is no evidence of adhesive lesions between the visceral pericardium and epicardium. The cause of effusive pericarditis is largely undetermined; on occasion it can be the result of slight leakage from the atria or ascending greater arteries. A recent pericardial effusion syndrome has been observed in adult horses in outbreaks of fetal loss and reproductive failure in Kentucky. It should be remembered that normally a small amount of pericardial fluid, ranging between 10 and 20 ml, should bathe the heart. The fluid is a thin lubricant and is light amber in color.

Fibrinous pericarditis

Fibrinous pericarditis in the horse morphologically resembles traumatic reticuloperitonitis of cattle. The pericardium is markedly distended by the presence of up to 10 liters of a thick, sero-fibrinopurulent exudate (Dill *et al.*, 1982). The inner surfaces of the pericardium and epicardium are covered by thick, shaggy layers of fibrin (Fig. 2). The material can adhere tightly to the epicardium. In cases of longstanding adhesive pericarditis, chronic constrictive heart failure results in fluid accumulation in the thorax, abdomen and pectoral subcutaneous tissues. Continued decrease of cardiac output in conjunction with diminished arterial perfusion and decreased venous return induces numerous irreversible biochemical and organ abnormalities.

The condition in the equine pericardial sac can be septic or aseptic. Bacterial isolates from the pericardium are usually *Actinobacillus equuli*, *Arcanobacterium pyogenes* and streptococcal species. Unlike traumatic pericarditis in cattle, the spread of *A. equuli* to the equine pericardium is believed to be the result of hematogenous infection. In adult horses, *A. equuli* has been identified as a common inhabitant of the tonsils and fecal contents. The affinity of *A. equuli* for the equine pericardium is unexplained.

In foals and neonates, disseminated, Gram-negative septicemia, such as occurs with salmonellosis or *Klebsiella pneumoniae* infection, can involve the pericardial sac as a fibrinous pericarditis. Hemopericardium (cardiac tamponade) should be considered as a differential diagnosis for effusive pericarditis. Several causes can

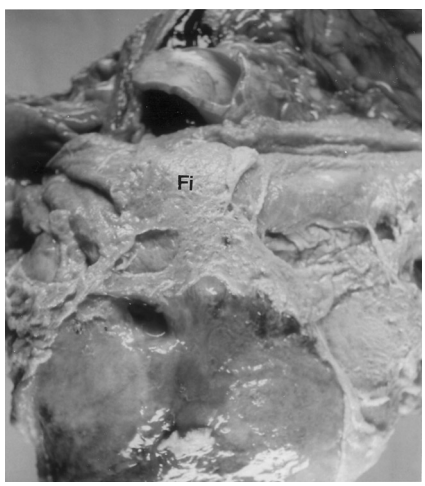

Fig. 2. Fibrinous pericarditis in a 6-year-old Arabian mare. Various layers of fibrin (Fi) cover the epicardium, giving it a shaggy appearance. *Actinobacillus equuli* was isolated from the pericardium.

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initiate cardiac tamponade in the horse, including aortic ring rupture, pulmonary trunk rupture and puncture wounds of the myocardium due to trauma (Fig. 3) or gunshots.

Pericardial tumors

In the horse, mesothelioma causing adhesive pericarditis has been diagnosed (Carrime *et al*., 1977); a case of pericardial hemangiosarcoma resulted in fatal thoracic hemorrhage (Birks and Hultgren, 1998).

Diseases of the myocardium

Diseases of the myocardium can generally be divided into primary necrotic–degenerative changes and primary inflammatory changes (Van Vleet and Ferrans, 1986). Infectious agents such as viruses, bacteria, fungi and parasites will contribute to primary inflammatory changes, whereas toxic, nutritional and biochemical disturbances will cause primary myodegenerative changes.

Primary myocardial degeneration

Nutritional

Lipidosis. This metabolic condition is associated with hyperlipidemia and hyperlipemia in ponies, donkeys and miniature horses and suggests disturbance of lipid metabolism (Platt and Whitwell, 1971; Mogg and Palmer, 1995). It has been reported as a negative energy balance resulting from feed restriction, pregnancy, lactation or disease-induced anorexia and stress. Multiple organs are involved in fatty metamorphosis, particularly the liver, but also the kidney and the heart. In cases of myocardial lipidosis, the cytoplasm of cardiac myocytes is infiltrated with discrete vacuoles, which stain positively for lipids.

Vitamin E/selenium-responsive disease. Nutritional myopathy (white muscle disease) is a degenerative disease that may affect the cardiac muscle of foals and young horses (Owen *et al*., 1977). The disease may even be present at birth. Vitamin E and selenium are essential elements to guarantee protection of cellular membranes from free radicals. Once the cell membranes have been damaged by free radicals, intracellular enzymes leak from the cell. Low levels of blood selenium or serum glutathione peroxidase may be indicators of deficiency of these nutrients. The disease presents as one of two clinical syndromes in equids: (i) acute and fulminate disease, which results in sudden death from heart failure; and (ii) subacute disease, leading to cardiac muscular weakness. Horses that survive the initial episodes will develop fibrotic scars in the myocardium.

The disease occurs when horses consume feed grown on selenium-deficient soils. Characteristic gross lesions at necropsy are pale, paintbrush white streaks or patches within the myocardium (Fig. 4). Histological changes reveal hyaline degeneration with fragmentation and lysis of myofibers (myocytolysis) in acute cases, with mineralization and histiocytic and sarcolemmal infiltrations in chronic cases.

Toxic

Monensin. Monensin is prescribed as a growth promoter for cattle and controls coccidiosis in poultry. Toxic myopathies can develop from monensin due to mixing error or unduly long storage of the ionophore in preparative equipment (Ordidge and Stoker, 1979; Amend *et al*., 1980; Muylle *et al*., 1981). The ionophore has a damaging effect on myocardial structures and function, causing cardiac arrhythmias and sudden death in affected horses. Horses are more sensitive to the toxic

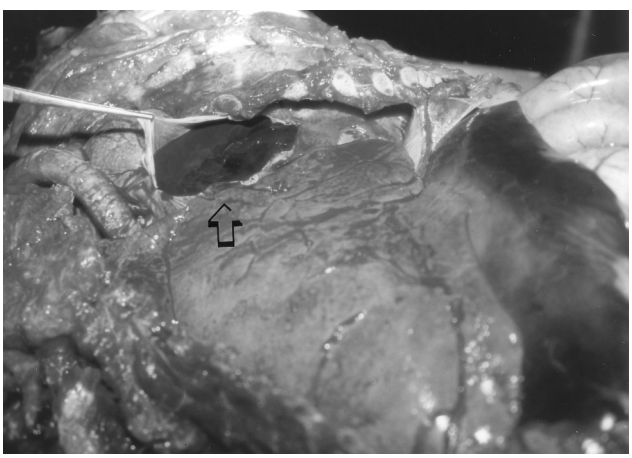

Fig. 3. Hemopericardium in a 4-day-old Thoroughbred colt. The pericardium, opened *in situ*, is filled with clotted blood (arrow).

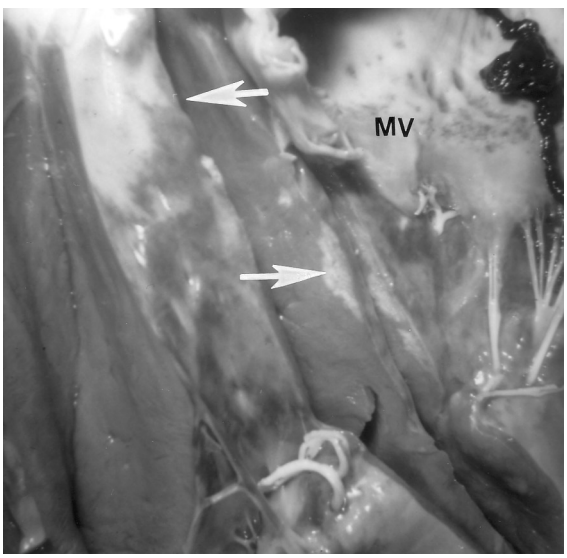

Fig. 4. Myocardial degeneration in a newborn foal. Patches of white tissue (arrows) occupy most of the left ventricular myocardium. This is an example of nutritional myodegeneration due to selenium/vitamin E deficiency. MV, mitral valve.

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effects of ionophore antibiotics than cattle, and hence consumption that may be safe for cattle may be liable to cause cardiac damage in the horse. Chronic cases may result in heart failure, pleural effusion and ventral edema. Grossly, the chronic changes are similar to those seen in nutritional myopathies. Acute histological changes are subtle and consist of segmental areas of myocytolysis, myocyte swelling, and vacuolar degeneration several days after consumption (Fig. 5). In chronic cases, myocardial fibers are replaced by fibrosis and collagen depositions. Mineralization is absent or less prominent. Myocardial changes of monensin toxicity are apparently not reparable. Biochemically, monensin interferes with membrane transport of sodium and potassium.

Cassia occidentalis (coffee senna). Coffee senna received its name because of the use of the bean as a substitute for coffee. The plant is an annual shrub native to the southeastern USA. The seedpods are brown when mature. The beans contain a toxic substance that targets cardiac and skeletal muscle mitochondria such that they undergo vacuolization, cytoplasmic swelling and separation (Hebert *et al.*, 1983). With the loss of mitochondrial energy production, cellular swelling results, with loss of glycogen and degeneration of the sarcolemmal system. Animals affected are mainly ruminants, though toxic episodes may occur in horses. Clinical signs include intravascular hemolysis, anorexia and diarrhea. Death follows recumbence by a few hours, and is due to heart failure. Gross lesions consist of focal or diffuse pallor or streaked, pale zones. Subepicardial hemorrhage may develop around the coronary arteries. Effusion into the pericardial sac occurs on occasions. Histological changes are similar to those seen with nutritional cardiomyopathy, but mineralization is not a feature.

Blister beetle poisoning. Although the disease has been mainly recognized in horses in Tennessee, Texas and Oklahoma, it may occur in any area where dead striped blister beetles of the genus *Epicauta* infest alfalfa hayfields (Schoeb and Panciera *et al.*, 1978, 1979; Helman *et al.*, 1997). Death is the result of cantharidin, a potent toxin produced by blister beetles in their hemolymph. Cantharidin is excreted by the equine kidney and can be detected in the urine. Cantharadin poisoning results from ingestion of alfalfa hay containing dead blister beetles. As little as 4–6 mg of beetle can kill a horse. In rare cases there is myocardial necrosis and hemorrhage in addition to the expected changes of mucosal acantholysis and vesicle formation in the gastrointestinal and urinary tracts. Histologically, myocyte fibers are swollen, lose their striations and become fragmented. Mineralization is not a common feature. A few neutrophils and extravasated red blood cells may be scattered between degenerated muscle fibers. It is believed that the myocardial damage is caused directly by cantharidin. Hypocalcemia and hypomagnesemia are severe metabolic dysfunctions. Individual bales of alfalfa harvested by cutting and crimping may contain blister beetles and when shipped out of state may cause unexpected poisoning in horses. It is important to identify the beetles and beetle parts in either the hay or the gastric contents of dead horses.

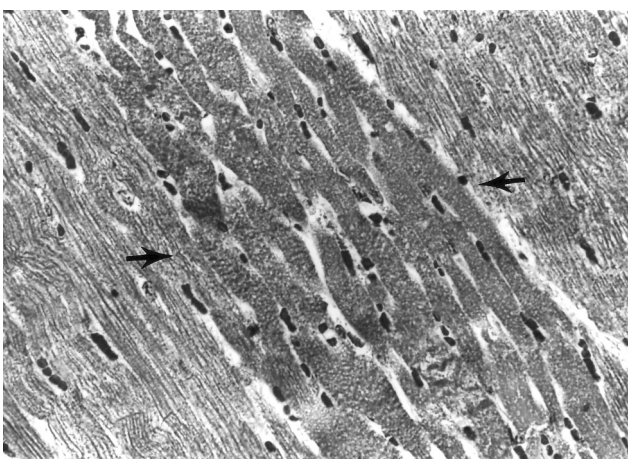

Fig. 5. Photomicrograph demonstrating toxic monensin myopathy in an adult horse. Bundles (arrows) of myocytes have a vacuolic sarcoplasm and have lost striations. Hematoxylin–eosin, ×40.

Oleander. The consumption of oleander (*Nerium oleander*) clippings has been associated with cardiac arrest and sudden death in livestock, including horses. Oleander is an extremely toxic plant. Pathological manifestations of oleander toxicosis associated with the heart reveal interstitial edema, hemorrhage and necrosis of myocytes. The diagnosis is established by identifying the ornamental shrub and by searching for oleandrin, a glycoside, by thin-layer chromatography of gastric or fecal contents (Galey *et al.*, 1996).

Aflatoxicosis. A variety of organs have been reported to be susceptible to the toxic effects of this mycotoxin in the horse, including the heart, where myocardial degeneration with lipid deposition can be present (Angsubhakorn *et al.*, 1981).

Catecholamine-induced myocardial necrosis. Catecholamine toxicosis, mainly reported in human cardiology but also in domestic animals, causes myodegenerative changes that are similar to those of vitamin E/selenium-deficient disease: swelling of myocytes, loss of striations, hypereosinophilia and mineralization. Sympathetic stimulation from primary central nervous system diseases apparently causes local overproduction of catecholamines in the myocardium, resulting in myocyte death. Various mechanisms have been proposed for the toxic effects of catecholamines (King *et al.*, 1982; Rona, 1985; Jiang and Dowling, 1990). Some of the incriminating factors are ischemia from vasoconstriction, increased calcium transport into myocytes, violent muscle contraction, excessive platelet aggregation and cytotoxic release of free radicals. The syndrome may occur in horses suffering from skull frac-

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tures, leading to intracranial hemorrhage and subsequent neurogenic myodegeneration (C.D. Buergelt, unpublished observation). Onset of myodegeneration typically occurs 3–4 days after central nervous system injury. Apparently there is a lag between the time of the initial nervous system insult and the development of observable myocardial lesions.

Primary inflammatory myopathies

Myocarditis

Myocarditis is a descriptive term meaning inflammation of the myocardium that is not typical of infarction. There is intense purulent or interstitial lymphocytic inflammation which may be diffuse or focal, and which may be associated with focal myocytolysis or focal myocyte necrosis. Primary inflammatory disorders causing myocarditis are relatively rare in horses (Fig. 6). *Streptococcus equi* has been reported to induce interstitial myocarditis, as has *Leptospira interrogans* in equine fetuses and stillborn foals (Poonacha *et al.*, 1993). In some instances of disseminated fungal infection, such as infection with *Aspergillus* sp., the myocardium may be seeded, and necrosis and inflammation ensues, with intralesional fungal mycelia (Fig. 7) present in these foci (Peet *et al.*, 1981). A recent case of *Halicephalobus gingivalis* infestation involved the myocardium as a multifocal granulomatous inflammation, in addition to the kidneys and the cerebellum (C.D. Buergelt, unpublished observation). Certain strains of equine infectious anemia virus and the viscerotropic strain of the virus of eastern equine encephalitis have been reported to induce acute interstitial lymphocytic myocarditis (Fig. 8), observed by microscopy (Rooney and Robertson, 1996). The etiology of chronic myocarditis in the heart of the horse remains largely undetermined (Fig. 9). Myocardial inflammation and fibrous scars may involve segments of the conducting system (Fig. 10) to induce disturbances, including sudden death.

Infarcts

Infarcts may develop in the myocardium from distant emboli showered into the coronary arterial circulation or from stenotic narrowing of the coronary arteries. Thus, vascular emboli in the myocardium or occlusive vascular phenomena are the prerequisite for the diagnosis of myocardial infarction. The types of myocardial infarctions so common in people are exceedingly rare in the horse. Myocardial infarctions do occur on occasion in the ventricular myocardium around the apex or in the right and occasionally the left atrium of the equine heart. It has been postulated that such infarcts are associated with migrating larvae of *Strongylus vulgaris*, causing the formation of thrombi and plaques within the sinus of Valsalva of the aortic semilunar valves or immediate ascending aorta and close to the coronary ostia (Farrelly *et al.*, 1954; Rothenbacher and Tufts, 1964; Cranley and McCullough, 1981). Another hypothesis

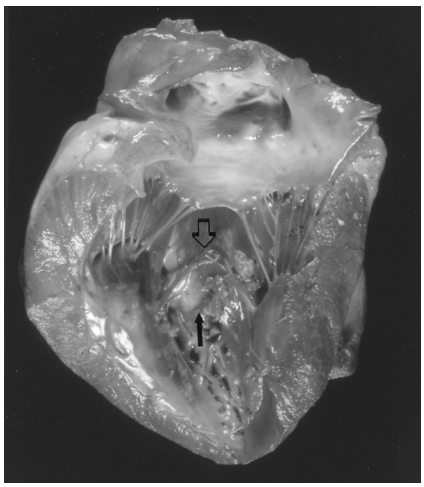

Fig. 6. Granulomatous myocarditis in a 10-year-old Quarter Horse gelding. Small white foci are present within the myocardium of the left ventricle (arrows).

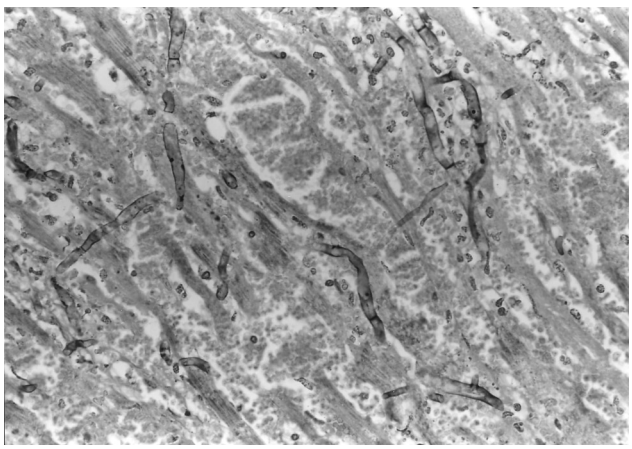

Fig. 7. Photomicrograph of myocardium showing aspergillosis in a 10-year-old Quarter Horse gelding. The necrotic myocardium is infiltrated by fungal hyphae that are segmented and occasionally branching. Hematoxylin–eosin, ×40.

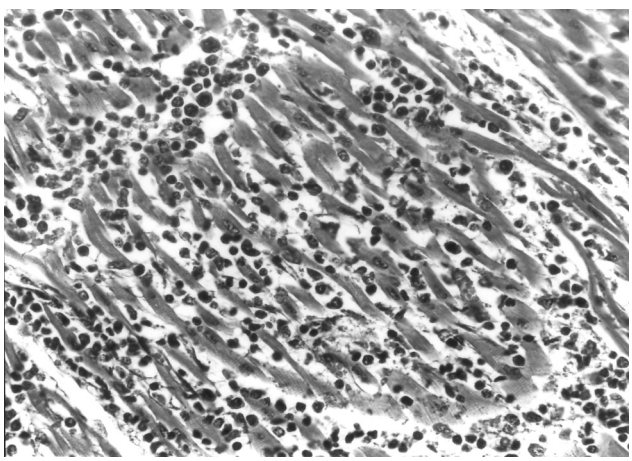

Fig. 8. Photomicrograph of myocardium showing lymphocytic myocarditis of undetermined cause in a 13-day-old Thoroughbred filly. The myocytes are diffusely infiltrated by small lymphocytes. Hematoxylin–eosin, ×40.

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proposed for myocardial scarring in the equine heart is that of coronary arteriosclerosis (Rothenbacher and Tufts, 1964). A detailed morphometric Swiss study on 68 hearts of horses, 6 months to 25.5 years of age, revealed that 79% had ventricular scars, compared with atrial scars in 7% of the hearts (Dudan *et al.*, 1984, 1985). Varying degrees of stenosing arteriosclerotic lesions within intramyocardial coronary arteries were considered to be responsible for the scars. Because of a lack of evidence, the authors ruled out the participation of *Strongylus* larvae in this process, and rather suspected a role for the neurovegetative system in the pathogenesis of the vascular alterations leading to ischemic conditions in the myocardium.

Trauma

Trauma to the chest leading to rib fractures over the heart of young horses or foals may on occasion result in cardiac tamponade due to heart puncture.

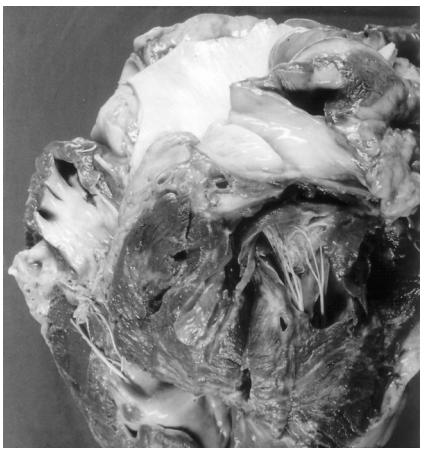

Fig. 9. Chronic myocarditis in a 32-year-old Tennessee Walking Horse mare. The entire myocardium is infiltrated by streaks and patches of collagenous tissue. The endocardium of the left ventricle is opaque as a result of fibrosis.

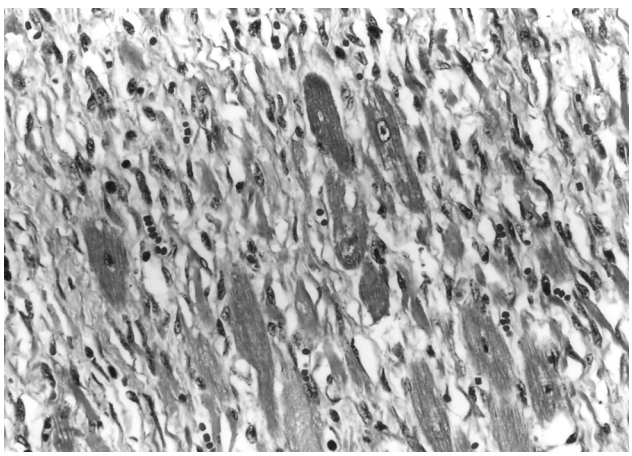

Fig.10. Photomicrograph showing chronic myocarditis in a 32-year-old Tennessee Walking Horse mare. Most of the myocardium has been replaced by collagen. Hematoxylin–eosin. ×40.

Cardiomyopathy

The condition seen mainly in human cardiology is defined as heart muscle disease of unknown origin (Gravanis and Ansari, 1987). Such cardiomyopathy apparently develops without preceding circulatory defects, valvular disease, pulmonary alterations or direct toxic or infectious insults to the myocardium. The end result is cardiomegaly and congestive heart failure. Three forms are distinguished in human cases: (i) dilated (congested); (ii) hypertrophic; and (iii) restrictive.

Cardiomyopathy (Figs 9 and 10) has not been well characterized in horses. Individual equine cases of either hypertrophic or dilated cardiomyopathies (Figs 11 and 12) leading to cardiomegaly, and the clinical signs of heart failure have been seen in referral institutions (Brumbaugh *et al.*, 1982; Bonagura, 1985; Nuytten *et al.*, 1988; Reef *et al.*, 1998; Davis *et al.*, 2002). The detailed clinical aspects of such heart conditions are beyond the scope of this article and are addressed in depth in textbooks of equine heart disease.

Diseases of the mural endocardium and valves

The endocardium is a thin, translucent connective tissue membrane that lines the ventricles, atria and valves. Diseases affecting the membrane can be degenerative, inflammatory or proliferative. In the horse, valvular alterations are more common than mural lesions (Else and Holmes, 1972a, b).

Endocardial fibrosis and calcification

Approximately 60% of horses over 20 years of age have some degree of focal thickening of the endocardium from fibrosis, most markedly in the region of the left ventricular apex. The affected endocardium is opaque and shows multiple folds or ridges. The changes indicate longstanding focal blood turbulence with permanent friction and irritation of the part of the endocardium that is involved. Unlike congenital fibroelastosis of the left ventricle, reported occasionally in young horses, the changes are incidental and do not result in congestive heart failure.

In congenital endocardial fibroelastosis, collagenous and elastic tissues diffusely thicken the entire left ventricle and left atrium. The thickened left ventricular endocardium prevents left ventricular contraction and blood output. The condition results in ventricular hypertrophy, cardiomegaly and congestive heart failure. The etiology of endocardial fibroelastosis has not been determined in animals. Three cases of endocardial fibroelastosis causing sudden death have been reported in the horse (Hughes and Howard, 1984; Belgrave *et al.*, 2002). Excessive elastic tissue involving the Purkinje fibers was responsible for the sudden death.

Metastatic mineralization occurs as a result of hypervitaminosis D_3 from toxic plants such as *Cestrum diurnum*

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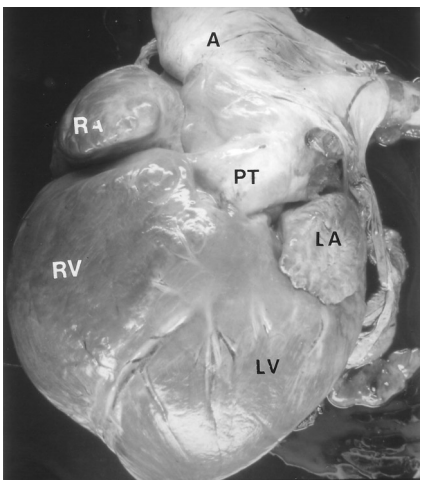

Fig. 11. Dilative cardiomyopathy in a 5-year-old male Thoroughbred. The heart has a globular appearance with both atria prominent. A, aorta; RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle; PT, pulmonary trunk.

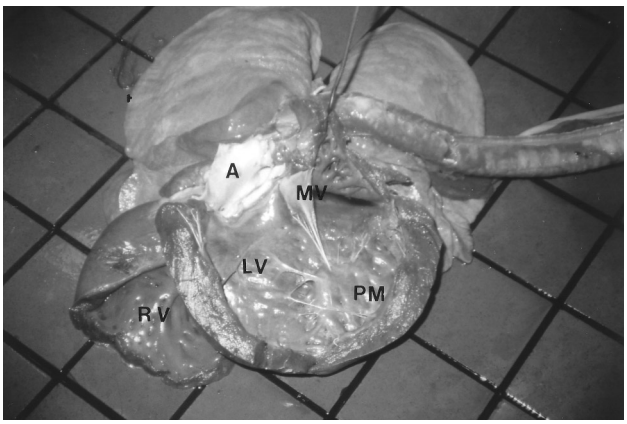

Fig.12. Dilative cardiomyopathy in a 5-year-old male Thoroughbred. The opened left ventricle has a flattened muscular profile that includes the papillary muscles. Lungs are attached. A, aorta; MV, mitral valve; RV, right ventricle; LV, left ventricle; PM, papillary muscle.

(Krook *et al.*, 1975) (Figs 13 and 14) or hypervitaminosis D from adding excessive vitamin D to the feed (Hasheck *et al.*, 1978). Tissue calcinosis is the result of hypercalcemia. Typically, the great arteries (Fig. 15) and other soft tissues (tendons and ligaments) are involved in a process of mineral salt deposition. Large, elevated, firm plaques cause roughening of the vascular intima, but thrombus formation is not a feature. The calcinogenic factor effective in *C. diurnum* toxicosis is $1,25(OH)_2D_3$ (Morris, 1982). Hypercalcemia and soft tissue mineralization can be associated with intestinal lymphosarcoma in the horse. In these cases calcification of endocardial surfaces of all four heart chambers, including the surface of the valvular cups, has been reported, together with plaques in the aorta (Mao *et al.*, 1990).

Fig. 13. Endocardial mineralization in a 2-year-old Paint gelding. Gritty plaques cover the endocardium of the entire left atrium (thick arrow) and portions of the subaortic ventricle (thin arrow). The condition developed from hypervitaminosis D due to chronic *Cestrum diurnum* toxicity.

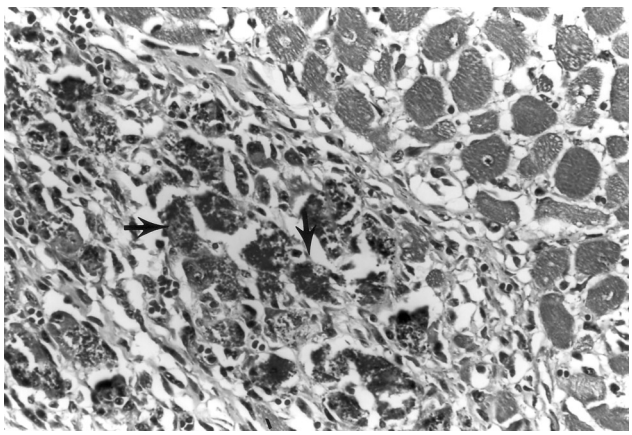

Fig. 14. Photomicrograph showing mineralization in the endocardium of a 2-year-old Paint gelding. Mineral granules are deposited along endocardial collagen fibers (arrows). Hematoxylin–eosin, ×40.

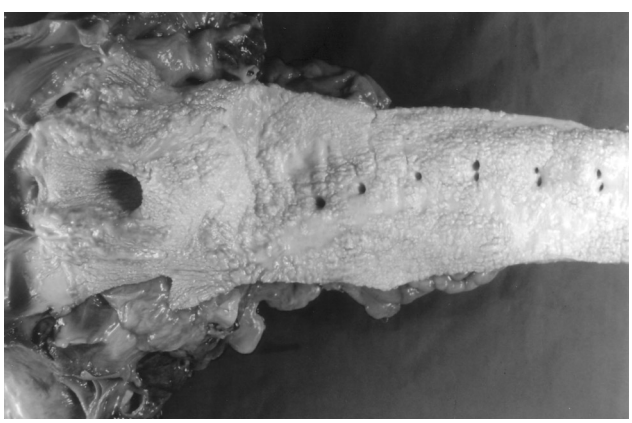

Fig. 15. Mineral deposits due to *Cestrum diurnum* in the ascending aorta of a 2-year-old Paint gelding. Toxicity diffusely thickens the intima.

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Endocarditis

Endocarditis, defined as inflammation of the endocardium, is the result of direct invasion by infectious agents or sensitization of the endocardium by predisposing factors such as bacterial toxins, leading to endothelial damage. Generally, valvular endocarditis is more common and critical than mural endocarditis.

In the horse, the valves of the left side of the heart are usually involved in endocarditis. The aortic valve is affected most frequently, followed by the mitral valve (Buergelt *et al.*, 1985). The different frequencies of endocarditis of the four valves may be related to the difference in the degree of pressure exerted on the valves, as increased pressure facilitates the entrance of bacteria (Nilsfors *et al.*, 1991). An alternative explanation for the varying degree of valvular preference for endocarditis, based on immunofluorescence studies in people is that it results from apparently uneven distribution of the number of immunoglobulin and C3b receptors in the human cardiac valve leaflets (Williams, 1987).

Valvular endocarditis occurs in acute, subacute and chronic forms. If infectious agents are isolated from the valve, the diagnosis of infective vegetative valvulitis is made (Fig. 16). The initial thrombus, made up of platelets and fibrin, grows from the addition of white blood cells (neutrophils, lymphocytes) and organizing granulation tissue, which forms from within the valve matrix (Fig. 17). Organisms isolated from cases of valvulitis in horses have been mainly *Streptococcus* sp. and *Actinobacillus equuli* (Buergelt *et al.*, 1985). In sporadic instances, Gram-negative organisms, such as *Pasteurella* sp., *E. coli*, *Serretia marcescens*, *Pseudomonas* sp. and fungi, have been isolated (Ball and Weldon, 1992; Ewart *et al.*, 1992; Pace *et al.*, 1994; Traavers and van den Berg, 1995; Maxson and Reef, 1997; Church *et al.*, 1998). The vegetation may be several centimeters in extent and may occupy the entire leaflet and more. Smaller lesions occupy the valvular margins, the ventricular surface of the semilunar valves or the atrial surface of the atrioventricular valves. Thrombotic involvement of chordae tendineae can occur from extension of valvular vegetations. Because of the friable texture of the vegetation, emboli are showered into the circulation to induce infarctions mainly in organs with a terminal arterial circulation, such as the kidneys.

One of the suggested reasons why lesions of the aortic valves are more common than lesions of any other valves in the horse is parasitism by *Strongylus vulgaris* larvae. Oddly, the larvae do not migrate beyond the aortic semilunar cusps and therefore the lesions caused by them are restricted to the inner endothelial surface of the valve leaflet and the intima of the aortic valve (Fig. 18). The incidental, clinically insignificant changes within the cusp or on the aorta are typically nodular and firm, and are sometimes calcified.

Valvular endocardiosis (fibrosis)

As an incidental finding at necropsy, mirror-image nodules have been described on the ventricular surface and

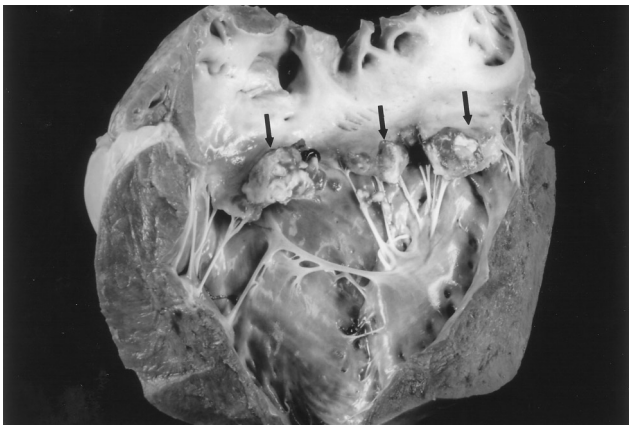

Fig. 16. Vegetative valvulitis in a 5-month-old Standardbred colt. Cauliflower-like, soft, grey material covers the leaflets of the mitral valve (arrows). *Streptococcus* sp. was isolated.

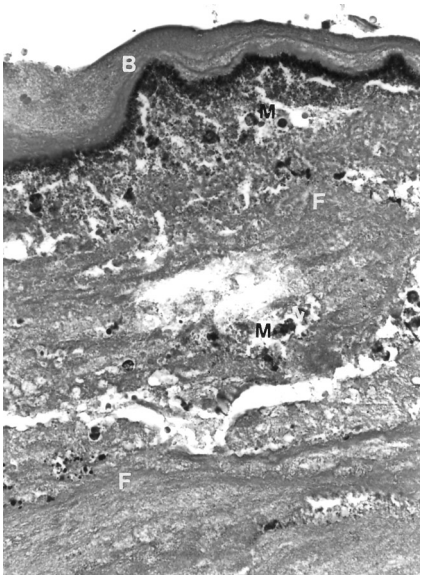

Fig. 17. Photomicrograph of valvulitis in a 3-year-old Thoroughbred stallion. The vegetation is composed of bacterial colonies (B), layers of fibrin (F) and foci of mineralization (M). Hematoxylin–eosin, ×20.

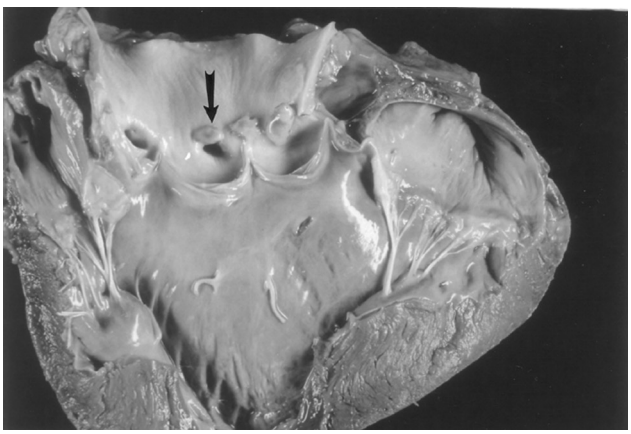

Fig. 18. Parasitic nodules in the aorta of an adult pony. Firm, smooth, mineralized nodules (arrow) arise from the intima, suggesting preceding larval migration of *Strongylus vulgaris.*

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at the edge of two cusps of the aortic semilunar valves. These are considered to be friction rubs, are covered by intact endothelium and have a core of fibrous tissue. Inflammatory cells are absent. The frequency of such nodules increases with age.

Fibrous thickening of the valvular matrix has been described in the atrioventricular valves of horses particularly in the mitral valves (Miller and Holmes, 1984, 1985; Schober *et al.*, 2000; Sage, 2002). The thickening can be diffuse (Fig. 19) and it may involve the free edge of the leaflet (Fig. 19). In either situation the covering endothelium remains smooth, glistening and intact. The hemodynamic complication is distortion of the valvular apparatus, leading to regurgitation of blood into the atrium. Fibrous thickening of chordae tendineae may ensue from extension of the process of valvular fibrosis. Histologically, an increased amount of loose, myxomatous connective tissue is present within the valvular matrix (Fig. 20). Inflammatory cells are absent. It has been suggested that the valvular changes in the horse are due to wear and tear or physical trauma during strenuous exercise as the valves collide with each other during the increase in blood pressure (Sage, 2002).

Rupture of chordae tendineae

There are three reports in the literature of chordal rupture in horses (Brown *et al.*, 1983; Holmes and Miller, 1984; Reef, 1987). All were associated with rupture of the main chordae of the mitral valve leaflets. The condition occurred from weakening of the caudal insertion at the site of the papillary muscle secondary to fibrosis or resulting from extension of valvular endocardiosis onto a shortened chorda. Ruptured chordae may be overlooked during routine dissection. The condition has been best characterized in man and dogs as a cause of mitral valve prolapse and severe acute fatal pulmonary edema.

Normal atrioventricular valve function depends on a geometric relation between the individual components of the valvular apparatus, namely the leaflets, chordae tendineae and papillary muscles. An abnormality of one or more of these components can produce valvular dysfunction or insufficiency. An affected horse may show clinical signs of exercise intolerance or poor performance from left atrioventricular valve regurgitation. Venous distension and ventral subcutaneous edema may develop from right atrioventricular valvular dysfunction.

Cardiac neoplasia

Cardiac neoplasias are extremely rare in the horse and when they occur are considered mainly to be secondary neoplasms showering the heart from another site. Metastasizing tumors in the equine heart are reported as multicentric lymphosarcomas (Neufeld, 1973; Weldon *et al.*, 1992) and hemangiosarcomas (Frye *et al.*, 1983). A lipoma infiltrative to the myocardium apparently arose from the adipose tissue of the coronary groove (Baker and Kreeger, 1987).

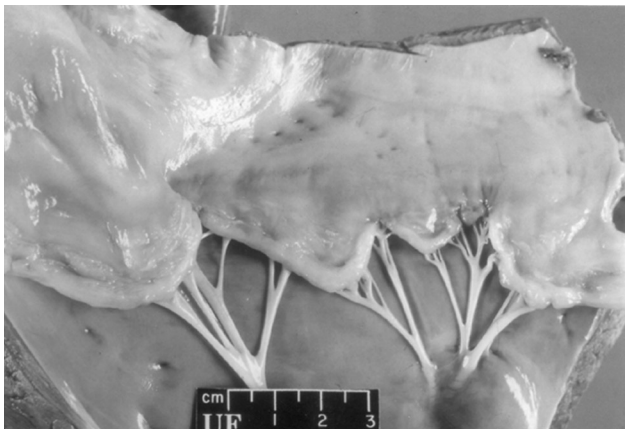

Fig. 19. Mitral valve fibrosis (endocardiosis) in a 4-year-old Thoroughbred mare. The entire leaflet and its free edges are thickened and opaque.

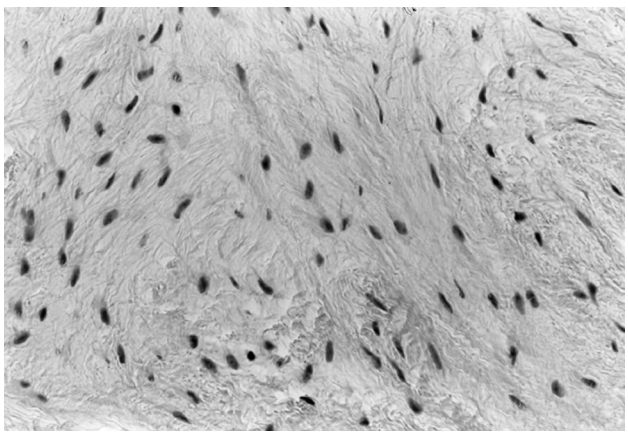

Fig. 20. Photomicrograph of endocardiosis in a 4-year-old Thoroughbred mare. The valvular matrix is largely composed of fibroblasts separated by a myxomatous stroma. Hematoxylin–eosin, ×100.

Sudden death and cardiac pathology

Healthy horses may collapse and die suddenly or be found dead unexpectedly. There are many potential causes for such equine sudden death scenarios (Baker and Ellis, 1981; Platt, 1982; Brown *et al.*, 1983; Gelberg *et al.*, 1985; Kiryu *et al.*, 1987; Dickenson *et al.*, 1996; Buergelt, 1999; Kiryu *et al.*, 1999). For the lay person, sudden death in a horse frequently leads to the assumption of a cardiac accident ('heart stroke') of some sort. A study of 69 equine cases of various breeds in the UK concluded that one-third of the cases of sudden death might have been due, in part, to intramyocardial hemorrhage or occlusion of coronary arteries (Platt, 1982). In racehorses studied for evidence of cardiac changes, inflammation or

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fibrosis associated with the conduction system (sinoatrial node, atrioventricular junction, bundle of His) were considered responsible for the sudden demise of some animals (Fig. 21). Presumably, such lesions led to bundle-branch blocks and the onset of fatal ventricular arrhythmias. In a series of 25 Thoroughbred race horses that died suddenly on the racetrack, only one horse had papillary muscle necrosis at necropsy (Gelberg *et al.*, 1985). The cause of death was undetermined in the majority of these cases after complete and thorough necropsy ('Swale syndrome') (Gelberg *et al.*, 1985). Cardiac arrhythmias were reported in one-third of the horses bitten by rattlesnakes (Dickenson *et al.*, 1996). Cardiac dysfunction and congestive heart failure resulted from myocarditis and myocardial scarring in the horses.

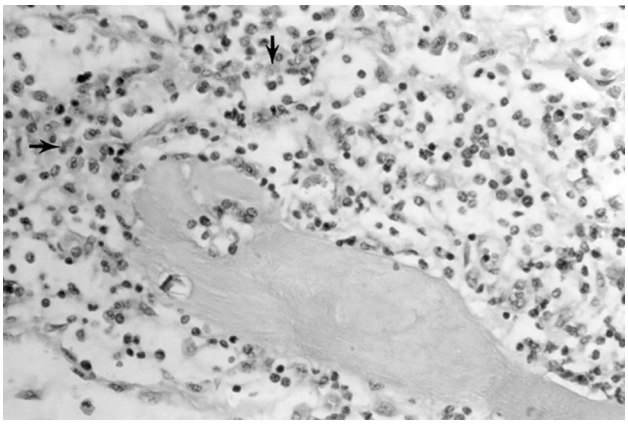

Fig. 21. Photomicrograph of the conduction system in a 4-year-old Andalusian stallion that died suddenly. There is subtle myocarditis. Lymphocytes, plasma cells and degranulated eosinophils (arrows) surround and focally infiltrate a Purkinje fibre. Hematoxylin–eosin, ×40.

Vascular diseases

Vasculitis

In horses, vasculitis is frequently associated with infectious agents such as viruses, bacteria, rickettsia and endoparasites.

Equine viral arteritis

An RNA virus belonging to the genus *Arterivirus* (family Arteriviridae) causes equine viral arteritis. The disease is clinically characterized by fever, depression, leukopenia and widespread edema, especially of the subcutis (Huntington *et al.*, 1990; Chirnside, 1992; DelPierro, 2000). Pregnant mares may abort. The virus damages endothelial cells directly, to cause panvasculitis of arteries, veins and lymphatics. Gross lesions include serositis and excess fluid accumulation in the chest, abdomen and pericardium. Microscopically, the disease is characterized by fibrinoid necrosis of the vessel wall with influx of lymphocytes and plasma cells. Equine viral arteritis should be differentiated from African horse sickness, equine infectious anemia, equine ehrlichiosis and purpura hemorrhagica.

Purpura hemorrhagica

Equine purpura hemorrhagica is an acute, necrotizing vasculitis that causes subcutaneous edema in the distal limbs, ventrum and head as well as subcutaneous and muscular hemorrhage. A gastrointestinal and renal component may be associated on occasion. Equine purpura hemorrhagica is believed to be an allergic reaction to streptococcal antigens, particularly to those of *Streptococcus equi*. Evidence indicates that sensitization to streptococcal antigen and subsequent immune-complex vasculitis is the pathogenetic basis for the disease (Galan and Timoney, 1985).

Rupture of major arterial vessels

In breeding stallions, a sudden death scenario is spontaneous rupture of the ascending aorta just above the aortic semilunar valve or within the aortic sinus of Valsalva (Sleeper *et al.*, 2001). Such a lesion will typically have a triangular-shaped tear with ragged edges. Ruptures affecting the pulmonary valves or pulmonary trunk are very rare.

If the rupture is within the valvular sinus close to the annulus fibrosus or if there is a direct tearing of the aortic ring (aortic cardiac fistula), frank hemorrhage may affect the interventricular myocardium. When the tear is higher, blood dissects into the pericardium, causing hemopericardium, or into the chest, causing hemothorax (Rooney *et al.*, 1967; Buergelt *et al.*, 1970; van der Linde-Sipman *et al.*, 1985; Reimer *et al.*, 1991). Elevated blood pressure and intra-aortic blood regurgitation, as well as weakening of the aortic wall in this region due to medianecrosis, are blamed for the sudden rupture by some authors.

In older horses the wall of the muscular major arteries undergoes degenerative transformation characterized by the formation of mucoid substances in the tunica media with foci of necrosis. The term 'cystic medianecrosis' has been applied (Buergelt *et al.*, 1970). Histologically, degenerative changes in the tunica media involve either the elastic lamina or the muscular lamina, or both. Ischemia is produced in the tunica media, leading to necrosis and tissue gaps. Mucinous substances, mainly composed of acid mucopolysaccharides, accumulate in the defects of the tunica media. Obliterative changes in the vasa vasorum are sometimes associated with the degenerative changes. It is believed that the degenerative condition weakens the vessel wall. A healthy major equine blood vessel is relatively resistant to high blood pressure.

Rupture of middle uterine artery

This phenomenon is usually seen in 12- to 21-year-old mares that have some complication with pregnancy or

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parturition. Severe exsanguinations into the broad ligament and uterine wall result from an aneurysmal rupture of the middle uterine artery. Degenerative, age-related changes in the wall of the vessel may predispose it to rupture under pressure from the weight changes that occur during pregnancy (Oikawa *et al.*, 1993). Again, medianecrosis is thought to be the underlying cause of such rupture. Others have suggested a related copper deficiency.

Verminous endoarteritis

One of the many different causes of equine recurrent colic is intestinal infarction secondary to thrombosis of the cranial mesenteric arterial root (Fig. 22) supplying the cranial mesenteric, ileocolic, cecal and colonic arterial system due to the presence of *Strongylus vulgaris* larvae (Wright, 1972; Georgi, 1973). Animals as young as 3 months can be affected (DeLay, 2001). In order to check for evidence of parasitic thrombosis, one must open the cranial mesenteric arterial root carefully before eviscerating the major abdominal organs. Two methods of approach and dissection can be pursued to examine the intima for defects. In one procedure the branches of the ileal, cecal and colonic arteries are identified *in situ*, lifted up with one hand and opened with long scissors by cutting towards the aorta. To obtain a clear view of the intima, one must avoid cutting into the adjacent caudal vena cava or portal veins. Employing the second method, the examiner opens the distal portion of the thoracic aorta with long scissors and continues within the aorta caudally through the diaphragmatic hiatus into the cranial abdominal aorta, opening the aortic orifice of the cranial mesenteric arterial root.

Fourth-stage larvae of *S. vulgaris* migrating along the intima of the cecal and colonic arteries against the blood flow towards the cranial mesenteric artery are the cause of the endoarteritis (McCraw and Slocombe, 1976; Morgan *et al.*, 1991; Hillyer and Mair, 1997). As the larvae undermine the intima they cause damage and defects to the endothelium and subsequent thrombosis, inflammation and fibrosis (Morgan *et al.*, 1991). The vascular lumen narrowing may vary among the involved vessels. As the inflammation progresses within the wall, the entire vessel may undergo destruction of muscle cells and elastic fibers, leading to the formation of aneurysms. Larvae can be identified within thrombi, or portions of larvae may extend into the vascular lumen. Resulting complications are emboli that are showered into the arterial circulation to induce signs of colic from intestinal infarction (Hillyer *et al.*, 1997) (Fig. 23). The same larvae may migrate up the aorta into the ascending aorta, where they die and become surrounded by thrombotic material, and induce the nodular changes in the intima of the ascending aorta or semilunar valves described earlier (Fig. 18). On the intimal surface the aorta may reveal threadlike elevations as traces of a fresh larval migration. Larval migration beyond the aorta is extremely rare and may involve the brain and spinal cord segments.

The inflammation may encroach upon the autonomic splanchnic ganglia that are normally located in the vicinity of the cranial mesenteric artery, causing intestinal dysperistalsis. On occasion, the verminous cranial mesenteric arterial root alterations may rupture to cause fatal hemoperitoneum.

Aortic–iliac thrombosis

This appears to be primarily a disease of racing Standardbred and Thoroughbred horses. There seems to be a greater incidence in male horses. The terminal aorta and its iliac branches at the quadrifurcation may develop a saddle thrombus (Fig. 24) that showers emboli into the arterial tree of the hind limb vasculature

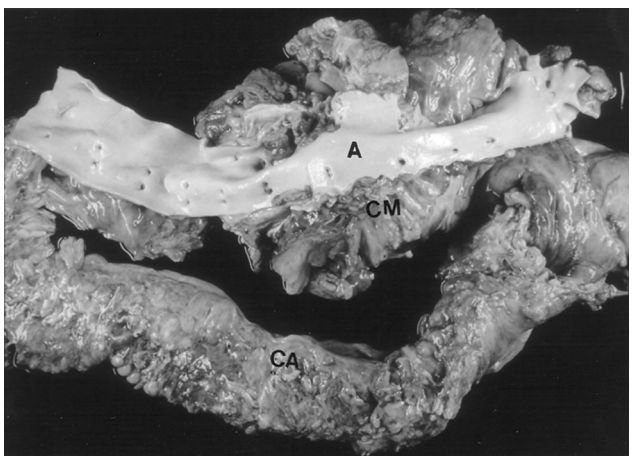

Fig. 22. Verminous endoarteritis of the cranial mesenteric artery in a 12-year-old Quarter Horse mare. The walls of the cranial mesenteric arterial root and of the entire tributary of the colonic artery have undergone chronic inflammatory changes (panarteritis) resulting from the migration of larvae of *Strongylus vulgaris*. A, aorta; CM, cranial mesenteric artery; CA, colonic artery.

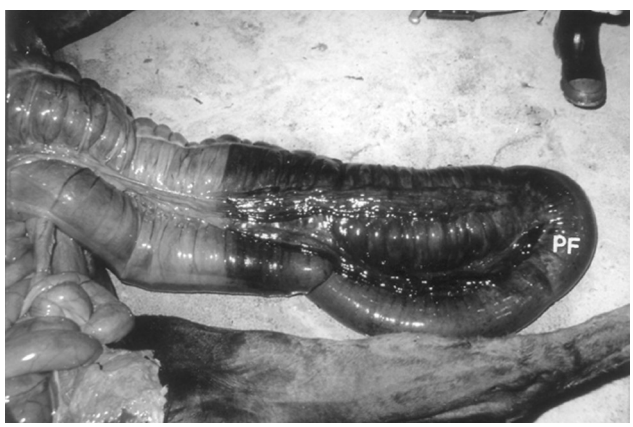

Fig. 23. Acute infarction in the pelvic flexure of a 12-year-old Quarter Horse mare. Thromboemboli showered from the site of verminous endoarteritis have occluded the colonic artery supplying the pelvic flexure (PF) of the colon, devitalizing the entire segment and inducing clinical signs of colic.

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(Crawford, 1982; Maxie and Physick-Sheard, 1985). Coldness of the affected limb, intermittent lameness and gait stiffness may be clinical signs associated with such thromboembolism. The thrombosed terminal aorta may be enlarged and firm on rectal palpation. Little is known about causes; unlike affected cats, dogs and humans, affected horses show no concurrent cardiomyopathy. The possible association with *Strongylus vulgaris* infestation and preceding endoarteritis of the cranial mesenteric artery as an initiating factor is intriguing but not proven. Fibrous intimal plaques at the site of thrombosis, hypercoagulability of the blood and damage to the aorta during vigorous exercise are other hypotheses proposed for the pathogenesis. Early cases of equine aortic–iliac thromboembolism had some morphological similarities to human arteriosclerosis (Maxie and Physick-Sheard, 1985).

Jugular vein thrombosis

Thrombophlebitis of one or both jugular veins is an iatrogenic event resulting from repeated short-interval intravenous injections. The thrombus may be septic, obstructing the entire vein. Venous distension proximal to the site of thrombosis is a clinical feature. Rarely do emboli sequester to shower the lungs. Non-septic thrombophlebitis resolves within several weeks and recanalization occurs. Collateral circulation may develop. In septic thrombosis, bacteria or fungi may colonize the vascular wall.

Carotid artery injection

Faulty intravenous injection may reach the adjacent, cervical muscle-protected carotid artery. In these instances, the applied medication will reach the brain and induce temporary or permanent damage. If this mistake occurs, it is necessary to search for the injection site and needle puncture by removing the alleged segment of the carotid artery for thorough inspection. This is not an easy task. On occasion, an intimal thrombus may be attached at the site of injection. This will be a good indicator of iatrogenic intimal damage, particularly if there is evidence of lines (striae) of Zahn (Fig. 25) on the thrombus surface created by the pulsating arterial blood over separating fibrin coagula and aggregated platelets. A perivascular hematoma associated with the injection site may be another indicator finding.

Hemomelasma ilei

An incidental finding at necropsy is the presence of discrete, black, pea- to walnut-sized plaques associated with the antimesenteric serosa of the terminal ileum (Fig. 26). The plaques are caused by microinfarcts of small mural arteries. Originally thought to be induced by migrating larvae of *Strongylus vulgaris* (Cohrs, 1961), they are particularly common in the ileum because the anastomoses between arterial branches are rare in this area. This hypothesis for the pathogenesis is not generally accepted. The black discoloration is from pseudomelanosis due to post-mortem bacterial production of hydrogen sulfide.

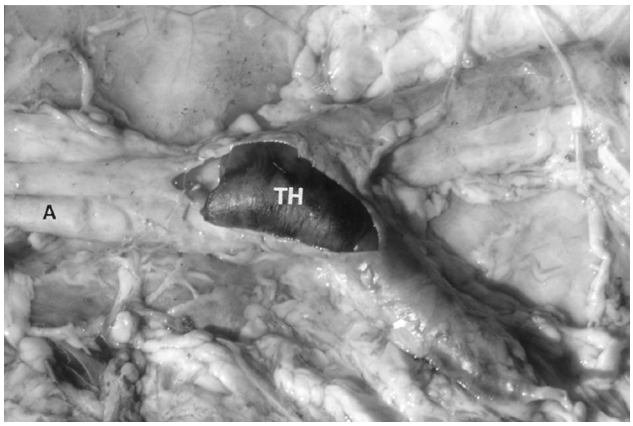

Fig. 24. Saddle thromboembolism in the terminal aorta of a 4-year-old male Standardbred racehorse. A large single thrombus has occluded and extended the lumen of the terminal aorta and the iliac arteries. A, aorta; TH, thrombus.

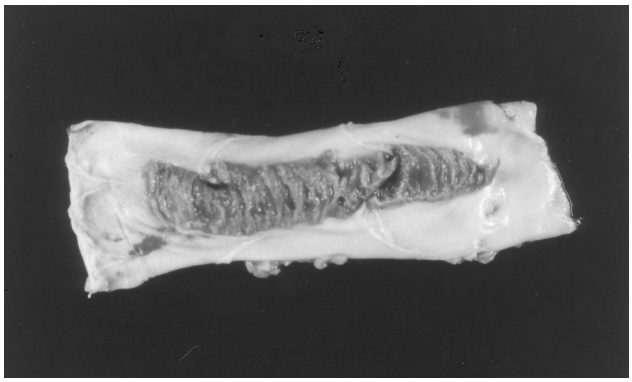

Fig. 25. Thrombus in the carotid artery of a 3-year-old Thoroughbred mare. The thrombus attached to the intima has a wavy profile from the pulsating intraluminal blood flow.

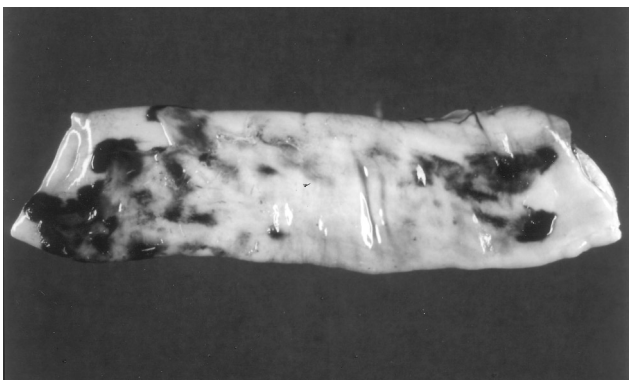

Fig. 26. Hemomelasma ilei in a 3-year-old male Thoroughbred. Several partially confluent bluish elevations are present on the surface of the antimesenteric serosa. The foci represent microinfarction of serosal blood vessels, leading to extravasation of erythrocytes.

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Intimal asteroid bodies

Intimal asteroid bodies are unique to the small arterioles of horses. Located in the subendothelium of blood vessels, they are considered to originate from degenerating components of vascular smooth muscle cells (Montali *et al.*, 1970; de Oliveira *et al.*, 1985). Asteroid bodies are found in horses aged 4 weeks or older and are widespread in all tissues. They are an indicator to pathologists that the tissue is of equine origin. Chemically, they are composed of calcium and phosphorus as the main elements (de Oliveira *et al.*, 1985).

Vascular neoplasia

Tumors of endothelial origin are classified as hemangioma when benign and hemangiosarcoma when malignant. The differential diagnosis includes tumor-like proliferation of mature vascular tissue, defined as hamartoma. Vascular tumors of the horse account for fewer than 1% of all tumors (Southwood *et al.*, 2000). Larger collections of equine hemangiosarcoma involved the respiratory and musculoskeletal systems, Thoroughbreds being over-represented (Sweeney and Gillett, 1989; Roussier *et al.*, 1990; Collins *et al.*, 1994). Other sites for hemangiosarcomas have been reported in the skin, eye and central nervous system (Hargis and McElwain, 1984; Hacker *et al.*, 1986; Bolton *et al.*, 1990; Berry, 1999).

Vascular tumors in the skin of young horses (16 months or younger) are often diagnosed as hemangiomas or angiomatosis (Johnson *et al.*, 1996). The tumors mainly occur in the skin of the extremities, and surgical treatment has proved curative. Again, such tumors have to be differentiated from hamartomas, a local overgrowth of mature tissue elements. Immunohistochemical demonstration of factor VIII-related antigen (VIII: Rag) is a histological marker of vascular endothelium and can be used as adjunct for the specific diagnosis of an endothelial-cell derived tumor (Johnson *et al.*, 1996)

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